Effects of Nicotine on Brain Metabolism

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Interest in the biochemical and anatomical mechanisms that are involved in the actions of psychoactive drugs, including nicotine, has led to studies on distributions of the functional responses to these drugs. Autoradiographic approaches that have been used in these studies include measurement of rates of cerebral blood flow and glucose utilization. The 2-deoxy-D-[1-^{14}C]glucose method of Sokoloff has been used to map and quantitate effects of various psychoactive drugs in the rat brain (1). The method allows simultaneous measurement of the regional cerebral metabolic rate for glucose (rCMRglc), an index of functional activity, throughout the central nervous system. It can provide information about the initial sites of drug interactions, and about the sites of secondary effects propagated via afferents to brain areas remote from the initial interactions.

The deoxyglucose method has been used to delineate the effects of nicotine treatments in the brain of the Fischer-344 rat (2,3). In rats subjected to acute systemic treatments with l-nicotine, the drug produces stimulation primarily in brain areas reported to contain specific binding sites for [^{3}H]nicotine, indicating that the sites are true receptors, which are linked to functional activity. Nicotine effects on rCMRglc are observed at doses of nicotine which are discriminated by the rat and which produce behavioral and physiological effects. The stimulation is transient, and is antagonized by mecamylamine. The brain areas affected include limbic structures, components of the visual system, brain stem nuclei which are important in cardiovascular reflexes, and several areas involved in motor function. The distribution of the in vivo effects of nicotine on rCMRglc implicates various brain regions in the behavioral and physiological effects of nicotine.

Chronic treatment of rats with nicotine produced rCMRglc effects which vary among brain regions (4). The ventral tegmental area, some components of visual pathways, the cerebellum, and vestibular nuclei show tolerance to nicotine challenge in rats given chronic nicotine. However, no regions shows sensitization to nicotine challenge.

The deoxyglucose method has been adapted for human studies with the use of 2-deoxy-2-[^{18}F]fluoro-D-glucose and positron emission tomography (PET) scanning. Using these procedures, the acute effects of euphorigenic treatments with morphine and cocaine have been studied in human volunteers (5,6). Ongoing studies are directed at relating the effects of intravenous nicotine on rCMRglc in smokers and nonsmokers with simultaneous effects on mood and feeling state. It is anticipated that these studies will help lead to a better understanding of brain mechanisms that which underlie the behavioral effects of nicotine and support the smoking behavior.

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